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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER
THOMAS, TIMOTHY P

ART UNIT	PAPER NUMBER
1614	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/578,765	DEDHIYA ET AL.	
	Examiner	Art Unit	
	TIMOTHY P. THOMAS	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 February 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-32 and 39-55* is/are pending in the application.

4a) Of the above claim(s) *8-11,23-25,27-32,42,43 and 45-55* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,12-22,26,39-41 and 44* is/are rejected.

7)☒ Claim(s) *17-22 and 44* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/3/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without specifying traverse of neramexane (the species of claim 12) as the compound of formula (I) (neramexane or a pharmaceutically acceptable salt thereof, recited in claim 12, are examined); and the aqueous composition of claim 44 (the aqueous composition comprises a) neramexane mesylate and b) purified water, USP, QS) in the reply filed on 2/14/2008 is acknowledged. The argument presented is on the ground(s) that the claims have been amended to require "preservative free" compositions, therefore the special technical feature has been modified to a preservative free aqueous-based composition. This is not found persuasive because the lack of unity determination was made with respect to the claim set on the record at the time of the previous Office Action, for which unity is lacking for the reasons of record. It is noted that even if the amended claim set were adopted for unity determination, unity is still lacking, as reflected by the prior art based rejections, which follow.

The requirement is still deemed proper and is therefore made FINAL.

2. Claims 8-11, 23-25, 27-32, 42-43, 45-55 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 2/14/2008.

It is noted that claims 17-22 optionally comprise the additives recited in these claims, which are not present in the elected aqueous composition specie; however, the

"optionally comprising" language also includes the embodiment where the recited additives are not present, which reads on the elected species. For this reason these claims are examined, to the extent they read on the elected species.

Priority

3. It is noted that this application appears to claim subject matter disclosed in prior Application No. 60/517981, filed 11/5/2003. A reference to the prior application must be inserted as the first sentence(s) of the specification of this application or in an application data sheet (37 CFR 1.76), if applicant intends to rely on the filing date of the prior application under 35 U.S.C. 119(e), 120, 121, or 365(c). See 37 CFR 1.78(a). For benefit claims under 35 U.S.C. 120, 121, or 365(c), the reference must include the relationship (i.e., continuation, divisional, or continuation-in-part) of all nonprovisional applications. If the application is a utility or plant application filed under 35 U.S.C. 111(a) on or after November 29, 2000, the specific reference to the prior application must be submitted during the pendency of the application and within the later of four months from the actual filing date of the application or sixteen months from the filing date of the prior application. If the application is a utility or plant application which entered the national stage from an international application filed on or after November 29, 2000, after compliance with 35 U.S.C. 371, the specific reference must be submitted during the pendency of the application and within the later of four months from the date on which the national stage commenced under 35 U.S.C. 371(b) or (f) or sixteen months from the filing date of the prior application. See 37 CFR 1.78(a)(2)(ii) and (a)(5)(ii). This time period is not extendable and a failure to submit the reference

required by 35 U.S.C. 119(e) and/or 120, where applicable, within this time period is considered a waiver of any benefit of such prior application(s) under 35 U.S.C. 119(e), 120, 121 and 365(c). A benefit claim filed after the required time period may be accepted if it is accompanied by a grantable petition to accept an unintentionally delayed benefit claim under 35 U.S.C. 119(e), 120, 121 and 365(c). The petition must be accompanied by (1) the reference required by 35 U.S.C. 120 or 119(e) and 37 CFR 1.78(a)(2) or (a)(5) to the prior application (unless previously submitted), (2) a surcharge under 37 CFR 1.17(t), and (3) a statement that the entire delay between the date the claim was due under 37 CFR 1.78(a)(2) or (a)(5) and the date the claim was filed was unintentional. The Director may require additional information where there is a question whether the delay was unintentional. The petition should be addressed to: Mail Stop Petition, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

If the reference to the prior application was previously submitted within the time period set forth in 37 CFR 1.78(a), but not in the first sentence(s) of the specification or an application data sheet (ADS) as required by 37 CFR 1.78(a) (e.g., if the reference was submitted in an oath or declaration or the application transmittal letter), and the information concerning the benefit claim was recognized by the Office as shown by its inclusion on the first filing receipt, the petition under 37 CFR 1.78(a) and the surcharge under 37 CFR 1.17(t) are not required. Applicant is still required to submit the reference in compliance with 37 CFR 1.78(a) by filing an amendment to the first sentence(s) of the specification or an ADS. See MPEP § 201.11.

Claim Objections

4. Claims 17-22 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

The language in claims 17 and 20, "optionally comprising" one or more of the agent recited in claims 17-22 does not require the presence of the agents of the instant claims, since they are optional, and therefore these claims do not further limit independent claim 1.

5. Claim 44 is objected to because of the following informalities: there are two periods in the claim, not at the end of the sentence, after a and b. Appropriate correction is required.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 22 and 44 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

With respect to claim 22, claim 20 recites the composition of claim 1 "optionally comprising" a solubilizer; however, claim 22 (depending indirectly on claim 21, which in turn depends on claim 20) recites "the composition of claim 21, wherein the glycerin is

present…" It is not clear whether the glycerin of claim 22 is required or is optionally present (not required), as in claims 20 and 21, rendering the claim indefinite.

With respect to claim 44, there is no conjunction (and / or) linking the components a and b; therefore it is not clear whether the recited components are both required (neramexane mexylate and purified water, USP,QS), or just one of the components (neramexane mexylate or purified water, USP,QS). For the purposes of prior art determinations, the 1st case is assumed (which will anticipate/obviate the 2nd case as well).

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 1-3, 6-7, 12, 14-22 and 39-40 are rejected under 35 U.S.C. 102(b) as being anticipated by Parsons et al. (WO 01/98253 A2; 2001 Dec).

Parsons teaches compositions that contain certain active 1-aminoalkylcyclohexane compounds (abstract); these active compounds include the elected compound, 1-amino-1,3,3,5,5-pentamethylcyclohexane (neramexane; p. 6, middle; p. 8, 1st named compound; p. 51 table, MRZ 579) and the HCl salt of neramexane (MRZ 2/579; p. 2, 1st named compound); the active compounds have a wide range of utility in the treatment of CNS-disorders (abstract); liquid compositions include solutions, suspensions, and capsules filled with the same for oral use (p. 21, last

2 lines – p. 22, 1st line); parenteral sterile solutions that include sodium chloride and double-distilled water q.s. according to conventional procedure, with aseptic filling into ampoules or IV-drip bottles (p. 23 paragraph (c)); drip solutions, injection and infusion preparations and the like (p. 23, 2nd paragraph); a solution for injection containing 12 mg active ingredient and sterile water to make 1 mL (12 mg/mL solution; p. 25, Ex. 4); liquid oral formulations and a TDS formulation that include active ingredient and purified water to give 2 mg/mL, 20 mg/mL and about 10 mg/mL of active ingredient (p. 26, Ex. 5-6; p. 27, Ex. 7; p. 28, Ex. 9); the 1 L volumes prepared in Examples 5-7 imply a container is used to hold these solutions, each of which would inherently hold a plurality of doses.

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

12. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of

the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

13. Claims 1, 4-5 and 39-41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Parsons et al. (WO 01/98253 A2; 2001 Dec).

Claims 1 and 39-40 are rejected as outlined above under 35 USC 102 (b). With respect to claims 4-5, Parsons does not teach aqueous neramexane compositions of about 4 mg/mL or about 5 mg/mL. Since Parsons does teach specific concentrations of 2, 10 and 20 mg/mL (see above) and unit dosages ranging from 1-1000 mg (p. 22, 4th line from bottom), substitution of 1-1000 mg into the 1 mg injection solution of Example 4 suggest solutions in the 1-1000 mg/mL range. Considering that specific concentrations of 2, 10 and 20 mg/mL are taught and a range larger than these values are suggested, it would have been obvious to one of ordinary skill in the art to prepare solutions with intermediate concentrations of about 5 mg/mL (half of 10) and 4 mg/mL (double 2). The motivation would have been routine optimization of concentrations of the aqueous compositions.

With respect to claim 41, Parsons does not teach a means for measuring a volume in the range from about 0.5 to about 10 mL. Since Parsons does teach aseptic into ampoules of intraveneous sterile solutions (p. 23, paragraph (c)), it would have

been obvious to one of ordinary skill in the art at the time of the invention to collect 30, 60 or 90 1 mL ampoules into a container (giving 30, 60 or 90 mL composition volume), packaged into a kit for a 30-day supply of once a day, twice a day or three times a day dosing, accompanied by a device for measuring (measuring means) and delivering the 1 mL volume taught by example 4. The motivation would have been to provide a 30-day sterile drug supply in a kit.

14. Claims 1, 13, 26, 44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Parsons et al. (WO 01/98253 A2; 2001 Dec) and Gupta et al. (US 2005/0014743 A1; priority 2003 May).

Claim 1 is rejected as outlined above under 35 USC 102 (b); Parsons teaches the active compounds are NMDS receptor antagonists (p. 1, 2nd paragraph), and are useful in treating CNS disorders (abstract). With respect to claims 13, 26 and 44, Parsons does not teach the mesylate salt of neramexane nor aqueous solutions containing a second active agent which is no a compound of instant formula (I). Gupta teaches various salts of NMDA antagonists can be used for treatment of depression and other mood disorders (paragraph 0065; title), a preferred salt is neramexane mesylate (paragraph 0065); neramexane mesylate is taught in combination with another antidepressant SSRI (active compounds effective in management of CNS-related conditions; claims 37-38; abstract). It would have been obvious to one of ordinary skill in the art at the time of the invention 1) to substitute the mesylate salt of neramexane for neramexane in aqueous solutions of neramexane and purified water, usp, qs, taught by Parsons, to give aqueous solutions of instant claims 13 and 44; and 2) to add either an

SSRI or an alternative CNS-effective compound to the aqueous neramexane solutions giving combinations of instant claim 44. The motivation 1) to use the mesylate salt would have been the art-recognized equivalent activity of the mesylate salt, which would be expected to be more soluble in aqueous solutions than neramexane. The motivation 2) to add a second active agent would have been 2a) the suggestion by Gupta of the combination of agents being useful for treatment of depression; or 2b) the combination of two compounds (the elected compound with another CNS active agent), in which both are art-recognized as effective in treatment of CNS disorders, potentially with complementary mechanisms.

Conclusion

15. No claim is allowed.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to TIMOTHY P. THOMAS whose telephone number is (571)272-8994. The examiner can normally be reached on Monday-Thursday 6:30 a.m. - 5:00 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on (571) 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Timothy P Thomas/
Examiner, Art Unit 1614

/Ardin Marschel/
Supervisory Patent Examiner, Art Unit 1614